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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/684,746	10/15/2003	Ravi V.J. Chari	A8658	4047

23373 7590 04/28/2005

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EXAMINER	
ANDERSON, REBECCA L	
ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 04/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	**Application No.** 10/684,746	**Applicant(s)** CHARI ET AL.
	Examiner Rebecca L. Anderson	**Art Unit** 1626

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 28 January 2005.
2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.
3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 53-70 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5)☒ Claim(s) 53-69 is/are allowed.
6)☒ Claim(s) 70 is/are rejected.
7)☐ Claim(s) _____ is/are objected to.
8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.
10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a)☐ All b)☐ Some * c)☐ None of:
1.☐ Certified copies of the priority documents have been received.
2.☐ Certified copies of the priority documents have been received in Application No. _____.
3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 28 Jan 05.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 53-70 are currently pending in the instant application. Claims 53-69 appear allowable over the prior art of record and claim 70, now rejoined, is rejected under 35 USC 112 1st paragraph.

Election/Restrictions

Claims 53-69 are directed to an allowable product. Pursuant to the procedures set forth in the Official Gazette notice dated March 26, 1996 (1184 O.G. 86), claim 70 directed to the process of making or using the patentable product, previously withdrawn from consideration as a result of a restriction requirement, is now subject to being rejoined. Claim 70 is hereby rejoined and fully examined for patentability under 37 CFR 1.104.

Response to Amendment and Arguments

Applicants' amendment to the claims and specification and the remarks filed 28 January 2005 have overcome the objection to the specification as introducing new matter, the rejection of claims 53-69 under 35 USC 112 1st paragraph as failing to comply with the written description requirement, and the 35 USC 112 2nd paragraph rejection of claims 53-69 as being indefinite. Therefore, since the product claims appear allowable, previously withdrawn claim 70 is rejoined and necessitates the following new 35 USC 112 1st paragraph rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

> art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 70 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method of inducing cell death in the cell populations of human squamous cancer, human breast tumors and Burkitt's lymphoma, does not reasonably provide enablement for the method of inducing cell death in all cell populations, for example, all tumor cells, virus infected cells, microorganism infected cells, parasite infected cells, autoimmune cells, activated cells, or any other diseased or abnormal cells The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

In _In re Wands_, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case,

The nature of the invention

The nature of the invention of claim 7 is the method of inducing cell death in selected cell populations comprising contacting target cells or tissue containing target cells with an effective amount of the cytotoxic composition of any one of claims 58, 59 or 60.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific diseases or affect what cell populations by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to therapeutic effects of the cytotoxic composition, whether the cell population is effected by the composition would make a difference.

Applicants are claiming a method of inducing cell death in selected cell populations comprising contacting target cells or tissue containing target cells with an effective amount of the cytotoxic composition of any one of claims 58, 59 or 60. As such, the specification fails to enable the skilled artisan to use the compositions of the formula (I) to induce cell death in any cell population, for example, in any tumor cells, virus infected cells, microorganism infected cells, parasite infected cells, autoimmune cells, activated cells, or any other diseased or abnormal cells. In regards to virus infected cells, for example, the obstacles to therapeutic approaches and vaccine development with regard to retroviruses associated with AIDS in humans are well documented in the literature. See, for example, Huff {J. Med. Chem. 34(8) 1991, p. 2305-2314} on page 2314. These obstacles include and are not limited to : 1) the extensive genomic diversity associated with HIV, particularly with respect to the gene encoding the envelope protein, 2) the fact that the modes of viral transmission include virus-infected mononuclear cells, which pass the infecting virus to other cells in a convert form, as well as via free virus transmission, 3) existence of a latent form of the virus, 4) the ability of the retrovirus to traverse the blood brain barrier and 5) the complexity and variation of the elaboration of the disease. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting therapeutic regimen on its face. In addition, there is no established correlation between in vitro activity and accomplishing treatment of viral infections, especially HIV infections, in vivo, and those skilled in the art would not accept allegations in the instant specification to be reliable predictors of success, and those skilled in the art would not be able to use the compounds of the formula (I) since there is no description of an actual method wherein a viral infection in a host is treated, i.e. there is no actual method wherein cell death is induced in a virus infected cell.

Applicants claims also include the method of inducing cell death in, for example, any tumor cell. The state of the prior art is that cancer therapy remains highly unpredictable. The various types of cancers have different causative agents, involve different cellular mechanisms, and consequently, differ in treatment protocol. It is known that the challenge of cancer treatment has been to target specific therapies to pathogenetically distinct tumor types, that cancer classification has been based primarily on morphological appearance of the tumor and that tumors with similar histopathological appearance can follow significantly different clinical courses and show different responses to therapy (Golub et al. page 531). Furthermore, it is known that chemotherapy is most effective against tumors with rapidly dividing cells and that cells of solid tumors divide relatively slowly and chemotherapy is often less effective against them. It is also known in the prior art (Lala et al. page 91) that the role of NO in tumor biology remains incompletely understood with both the promotion and inhibition of NO mentioned for the treatment of tumor progression and only certain human cancers may be treated by selected NO-blocking drugs. These example shows that there are different cellular mechanisms, the unpredictability in the art and the different treatment protocols.

Hence, one of skill in the art is unable to fully predict possible results from the administration of the compound of the claims.

The amount of direction or guidance present and the presence or absence of working examples

The only direction or guidance present in the instant specification is a general listing of cell populations on page 7, including, for example, tumor cells, virus infected cells, microorganism infected cells, parasite infected cells, autoimmune cells, activated cells, or any other diseased or abnormal cells. Page 22 lists various diseases applicant considers treatable by administering the cytotoxic composition, for example, HIV and a multitude of cancers. The only exemplary data is found on page 23 for the in vitro induction of cell death for Burkitts Lymphoma, human breast tumor and human epidermoid carcinoma and on page 32 for the in vivo treatment of human squamous cancer by inducing cell death in human squamous cancer cell populations. There are no working examples present for the induction of cell death in any other diseased or abnormal cells, such as microorganism infected cells, parasite infected cells, autoimmune cells, virus infected cells, activated cells, etc.

The breadth of the claims

The breadth of the claims is the method of inducing cell death in selected cell populations which includes, for example, any diseased or abnormal cells, such as tumor cells, virus infected cells, microorganism infected cells, parasite infected cells, autoimmune cells, activated cells, which includes the treatment of any cancer and HIV, for example.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what cell populations out of all cell population the cytotoxic composition could be administered to induce cell death and to determine what the benefited (i.e. treatment of HIV) would and would furthermore then have to determine which of the claimed compounds would provide treatment of which disease, if any and which compounds would induce cell death in which cell populations..

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the cytotoxic composition for the method of inducing cell death in any cell populations. As a result necessitating one of skill to perform an exhaustive search for which cell populations can be treated by what compositions of the instant claims in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search , but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test the method encompassed in the instant claims, with no assurance of success.

This rejection can be overcome, for example, by deleting the claim or by inserting the supported cell populations, i.e. -- a method of inducing cell death in human squamous cancer cell populations comprising contacting human squamous cells or tissue containing human squamous cells with an effective amount of the cytotoxic compositions of any one of claims 58, 59 or 60.--

Conclusion

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rebecca L. Anderson whose telephone number is (571) 272-0696. Mrs. Anderson can normally be reached Monday through Friday 5:30AM to 2:00PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Joseph K. McKane, can be reached at (571) 272-0699.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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